

The University of Chicago

THE VELOCITY OF HYDROLYSIS OF
STEREOISOMERIC HYDRAZONES
AND KETAZINES

A DISSERTATION SUBMITTED TO THE
FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1938

By

EVERETTE ASKINS SLOAN

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All studies in stereo-isomerism date from 1848 when Pasteur presented his historic paper¹ before the French Academy on the isomeric tartaric acids. Wislicenus² in 1873 pointed out optical relationships in lactic acid similar to those observed by Pasteur in tartaric acid, and came to the striking conclusion that the facts force us to explain the difference between isomeric molecules of the same structure by a different arrangement of the atoms in space.

The situation was clearly elucidated in 1874 by the memorable papers of van't Hoff³ and Le Bel.⁴ These investigators working separately proposed simultaneously the theory of spacial molecular asymmetry. They suggested that the four valences of carbon are distributed about the atom as at the corners of a symmetrical tetrahedron and that two isomeric molecules may be expected when this central atom is joined to four different radicles. These findings and principles have been thoroughly confirmed by hundreds of investigators since that time and remain as the foundation of the science of stereo-chemistry.

Isomerism Involving the Carbon-Nitrogen Double Bond

Hantzsch and Werner were the first to suggest the application of the ideas of van't Hoff and Le Bel to the explanation of the isomerism noticed by Victor Meyer and Goldschmidt⁵ in the oximes. Following up his work on nitro paraffins Meyer had been led to investigate the action of hydroxyl amine on ketones and aldehydes. In this Meyer⁶ first prepared and described the oximes of acetone, methylethyl ketone, acetophenone, benzophenone, chlo-

¹Pasteur, Ann. chim. phys., (3) 24, 442 (1848).

²Wislicenus, Ann., 167, 343 (1873).

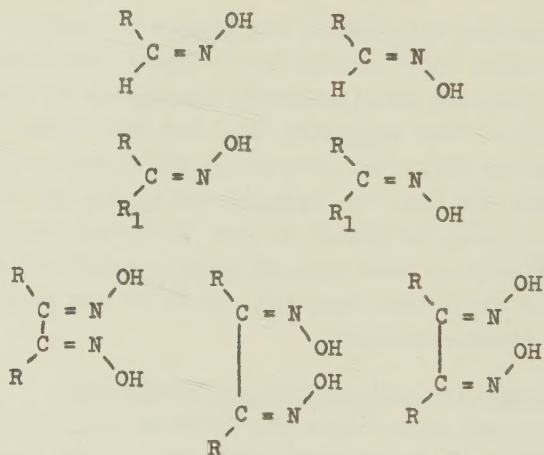
³van't Hoff, Bull. soc. chim., 23, 295 (1875).

⁴Le Bel, Bull. soc. chim., (2) 22, 337 (1874).

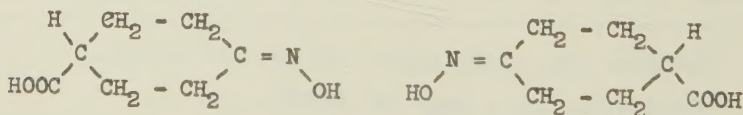
⁵Goldschmidt and Meyer, Ber., 16, 1616, 2176 (1883).

⁶V. Meyer, Ber., 15, 2778 (1882).

ral, and acetaldehyde. While pursuing the reaction further he and Goldschmidt observed two forms of benzildioxime. Later he and Auwers⁷ isolated the third isomer of this material. In seeking to explain this isomerism Hantzsch and Werner⁸ pointed out: (1) that in trivalent nitrogen the valences do not lie in the same plane, but form a tetrahedral structure with the nitrogen atom at one of the corners, (2) that the double bond between carbon and nitrogen in the oximes prevents free rotation at that position, and (3) that the position of the -OH radicle with respect to the rest of the molecule accounts for the isomerism of the oximes formed from aldehydes and unsymmetrical ketones.



The works of Mills and Bain⁹ seem to prove definitely the non-planar structure of trivalent nitrogen in oximes. They were able to resolve the oxime of cyclohexanone-4-carboxylic acid into optically active isomers.



From the nature of the groups syn and anti forms of this oxime

⁷Auwers and Meyer, Ber., 21, 788 (1888); 22, 709 (1889).

⁸Hantzsch and Werner, Ber., 23, 21-25, 1250 (1890).

⁹Mills and Bain, J. Chem. Soc., 97, 1866 (1910).

would not be expected. But the existence of enantiomorphic modifications of this substance clearly indicates the tetrahedral valences of nitrogen here.

The expected number of isomeric oximes, based on the Hantzsch-Werner theory, has been prepared from a large number of aromatic aldehydes, ketones, and diketones.¹⁰ But from the purely aliphatic aldehydes and ketones very few isomeric oximes have been separated. A variety of substances other than oximes containing the carbon-nitrogen double bond have been prepared in the syn and anti isomeric forms. Examples of these are to be found in the semicarbazones and thiosemicarbazones,¹¹ anils,¹² chlorimides,¹³ osazones,¹⁴ phenylhydrazones,¹⁵ and simple hydrazones.¹⁶

Configuration of Compounds containing the Carbon-Nitrogen Double Bond

For many years the configurations of the oximes as postulated by Hantzsch¹⁷ remained unchallenged. His ideas were based on the behavior of the acetate derivatives of the isomeric aldoximes in the presence of dilute NaOH at room temperature. The acetate from the form of the oxime designated anti by Hantzsch is

¹⁰A. Werner, "Lehrbuch der Stereochemie," Jena, 1904, pp. 225-66.

¹¹Wallach, Ber., 28, 1955 (1895); Knoevenagel and Goldschmidt, Ber., 31, 2474 (1898); Posner, Ber., 34, 3979 (1901); Busch, J. prakt. Chemie, 83, 425 (1911); Ibid., 93, 339 (1916); Wilson, J. Chem. Soc., 105, 2892 (1914); Ibid., 125, 841 (1924).

¹²Simon, Compt. rend., 118, 1345 (1894); Miller and Plöchl Ber., 27, 1296 (1894); Eibner and Peltzer, ibid., 33, 3461 (1900); Hantzsch, Ber., 34, 822 (1901); Busch, Ber., 43, 2557 (1910).

¹³Stieglitz, Amer. Chem. J., 18, 751 (1896); Ibid., 30, 399 (1903); Hilpert, ibid., 40, 155 (1908); Stieglitz and Peterson, Ber., 43, 782 (1910); Peterson, Amer. Chem. J., 46, 325 (1911).

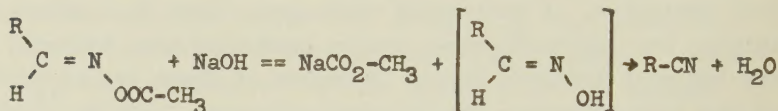
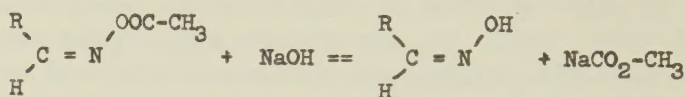
¹⁴Anschutz, Ber., 28, 64 (1895); Ingle, Proc. Chem. Soc., 67, 111 (1895); Blitz, Ann., 305, 179 (1899); Ibid., 308, 7 (1899); Ibid., 321, 1 (1902); Fromm, ibid., 394, 310 (1912).

¹⁵E. Fischer, Ber., 29, 793 (1896); Auwers and Meyer, Ber., 24, 4226 (1891); Claus, J. prakt. Chemie, 45, 377 (1892); A. Werner, "Lehrbuch der Stereochemie," Jena, 1904, pp. 267-68, for many other references.

¹⁶Chuang, Abstract Thesis, The University of Chicago Science Series, 1924-25, III, 111-18; Xanthopoulos, ibid., 1925-26, IV, 195-201.

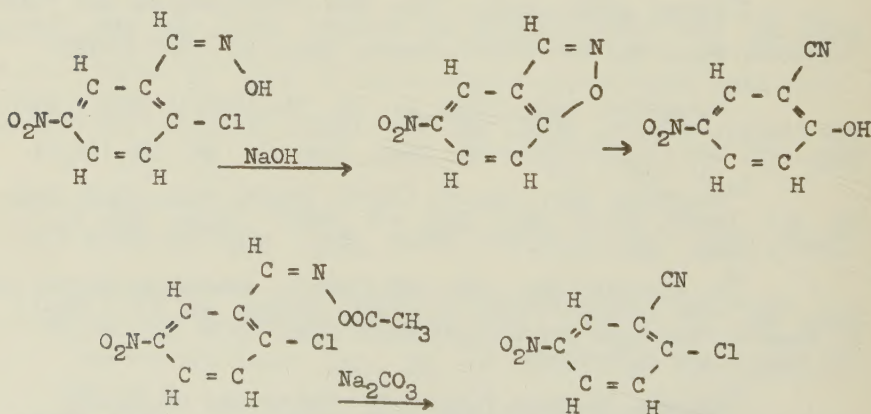
¹⁷Hantzsch, Ber., 24, 13, 22 (1891).

readily hydrolyzed by dilute NaOH to the original oxime. While the corresponding derivative of the syn form is converted into the nitrile through the loss of the elements of acetic acid.



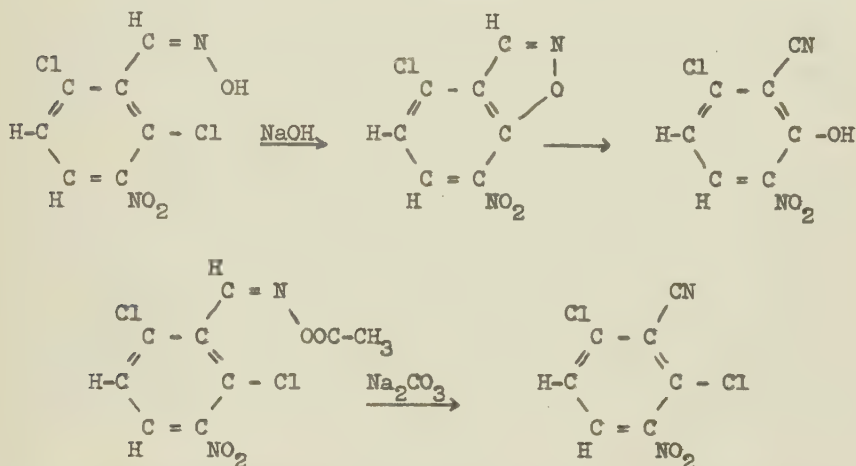
Hantzsch assumed that the syn-form of the oxime should eliminate the elements of water more easily than the anti-form.

More recent works of Meisenheimer, Brady and Bishop and others seem to indicate that it is the anti-form of the oxime that undergoes the loss of water with the formation of the nitrile. According to Brady and Bishop¹⁸ the alpha form of 2-chloro-5-nitrobenzaldoxime remained unchanged on boiling with normal NaOH for 30 minutes. The other isomer, or beta form, of this oxime was easily converted into the corresponding nitro derivative of salicylo-nitrile through the loss of HCl. And further the acetate of this beta form was readily decomposed to the nitrile in the presence of Na₂CO₃. This indicates that the beta form has the -OH proximate to the benzene ring and loses water more readily. See structures below.



¹⁸Brady and Bishop, J. Chem. Soc., 127, 1357 (1925).

Meisenheimer and Theilacker¹⁹ obtained similar results working with the isomeric forms of 3-nitro-2,6-dichlorobenzald-oxime. From one form of this oxime (anti according to Hantzsch or beta according to Brady) they obtained 6-chloro-3(or 5 ?)nitro-2-hydroxybenzonitrile by treating with cold 0.25 N NaOH for 24 hours. The acetate of the beta oxime was also unstable in the presence of Na₂CO₃ and was readily changed to the nitrile. Neither the alpha (or syn) form of the oxime nor its acetate was converted into the nitrile by this treatment.

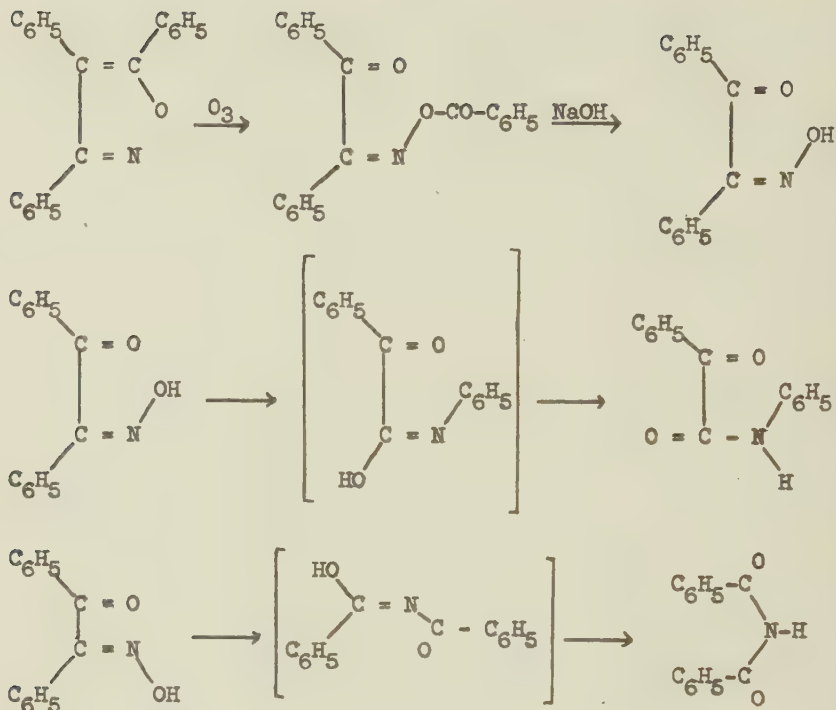


Meisenheimer²⁰ has also done significant work in the identification of the unsymmetrical ketoximes. He demonstrated that one form (the beta) of benzilmonoxime could be prepared from 3,4,5-triphenylisoxazole by oxidation to the benzoyl derivative of the benzilmonoxime and hydrolyzing. The same benzoyl derivative was prepared by the benzylation of the beta oxime. This would indicate that the -OH radicle in the beta benzilmonoxime is anti with respect to the phenyl. He then showed²¹ that the beta benzilmonoxime when subjected to the Beckmann rearrangement was converted into the anilide of benzoylformic acid, while the alpha isomer rearranged to form dibenzoylimide. From these reactions somewhat

¹⁹Meisenheimer, Theilacker, and Beisswenger, Ann., 495, 249 (1932).

²⁰Meisenheimer and Weibezahn, Ber., 54, 3195 (1921).

²¹Meisenheimer, Ber., 54, 3206 (1921).



general methods have been formulated for establishing the configurations of the unsymmetrical ketoximes. It is generally considered that there is a trans-migration of the radicals in the Beckmann rearrangement.*

*The striking success of the Hantzsch-Werner theory in predicting the true number of isomers in many compounds containing the carbon-nitrogen double bond encouraged research in the attempt to separate optical isomers in the trivalent nitrogen compounds where three different (but inactive) radicals are joined to the nitrogen atom.



But it seems that all attempts to resolve such tertiary amines and their substituted derivatives have been unsuccessful:

N-methyl-N-ethyl sulfanilic acid²²

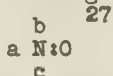
²²Jones and Millington, Proc. Cambridge Phil. Soc., 12, 489 (1904).

Although a large number of isomers (syn and anti) have been found in different types of compounds containing the carbon-nitrogen double bond, no significant results seem to have been obtained on the configuration of such isomers other than oximes. Certain differences between the stable and labile forms are more or less general, and in some cases give indication of the configurations. The stable form has been found to have the higher melting point, to be less soluble, to have a higher refractive index,²⁸ higher viscosity,²⁹ and higher dipole moment.³⁰ In the case of some aldioximes Brady³¹ showed that the lower melting isomer had the greater dissociation constant as an acid. Chuang³² who first prepared the isomeric p-methoxybenzophenone hydrazones attempted

N-phenyl-N-p-tolyl anthranilic acid²³
Methyl-benzyl-hydroxyl amine²⁴

The failure to resolve such compounds does not discredit the original tetrahedral structure of the nitrogen atom for enantiomorphic forms of such trivalent nitrogen compounds might be very easily racemized.

The successful resolution of the quaternary ammonium salts with four different but inactive groups attached to the nitrogen was first partially accomplished by Le Bel²⁵ in 1891 and later by Pope and Peachey²⁶ and many others. Such findings and the work of Meisenheimer in resolving the tertiary amine oxides,



firmly establish the tetrahedral structure of the valences of nitrogen.

²³Meisenheimer, Angermann, Finn, and Vieweg, Ber., 57, 1745 (1924).

²⁴Denner, Diss., Tübingen (1930).

²⁵Le Bel, Compt. rend., 112, 724 (1891).

²⁶Pope and Peachey, J. Chem. Soc., 75, 1127 (1899).

²⁷Meisenheimer, Ber., 41, 3966 (1908).

²⁸Beckmann, Ber., 23, 1686 (1890); Auwers, ibid., 57, 446 (1924).

²⁹Thole, J. Chem. Soc., 101, 552 (1912).

³⁰Sutton and Taylor, J. Chem. Soc., 2190 (1931).

³¹Brady, J. Chem. Soc., 1918 (1926).

³²Chuang, Doctorate Dissertation, University of Chicago (1924).

their rearrangement but could observe no difference in their reaction. Johnson³³ observed that the beta-p-methoxybenzophenone oxime showed a higher rate of hydrolysis than the alpha isomer, but was unable to detect any appreciable difference in the rates of hydrolysis of the two isomeric hydrazones.

Hydrolysis of Compounds containing the Carbon-Nitrogen Double Bond

The hydrolysis of oximes, hydrazones, semicarbazones and other compounds containing the carbon-nitrogen double bond proceeds smoothly in the presence of strong acids. In such cases the ketone or aldehyde is regenerated together with the salt of the hydrazine, hydroxyl amine or semicarbazide. The formation of the oximes, hydrazones and semi-carbazones seems to be favored by weakly basic solutions. A number of papers have appeared on the investigation of the equilibria involved.



Acree and Johnson³⁴ studied the rate of formation of acetoxime and reported that both the forward and reverse reactions were catalyzed by hydrochloric acid. Bartlett and Lapworth³⁵ investigating the same reaction found that the formation of the oxime was catalyzed by either acid or base but that the formation of oxime fell off rapidly when the acid was present greater than 0.6 equivalent in 40 liters containing one mole of each reactant. Ardagh and Williams³⁶ determined the percentage acetone-phenylhydrazone present at equilibrium at different concentrations of hydrogen or hydroxyl ion. A maximum of approximately 90 per cent hydrazone was present at pH 6.0--6.6, but only about 15 per cent hydrazone was present with an acid concentration of 0.02 N. Conant and Bartlett³⁷ made a comprehensive study on semi-carbazone formation in phosphate buffered solutions. The equilibrium constants and the rates of formation and hydrolysis for a number of semi-carbazones were evaluated.

³³Johnson, J. Am. Chem. Soc., 56, 1904 (1934).

³⁴Acree and Johnson, Am. Chem. J., 38, 308 (1907).

³⁵Bartlett and Lapworth, J. Chem. Soc., 93, 85 (1908).

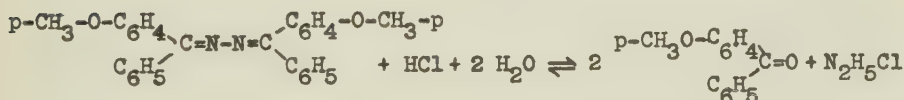
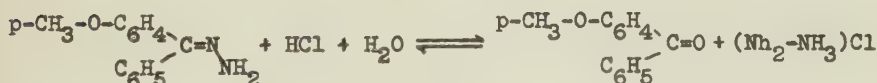
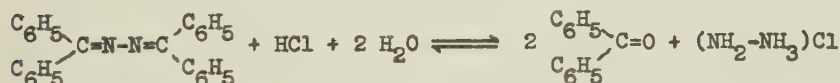
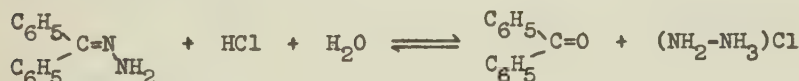
³⁶Ardagh and Williams, J. Am. Chem. Soc., 47, 2976 (1925).

³⁷Conant and Bartlett, ibid., 54, 2881 (1932).

All the literature indicates extensive hydrolysis of these compounds in highly acid solutions.

The Problem of this Research

The object of this research was (1) to further investigate the rates of hydrolysis of the isomeric alpha and beta-p-methoxybenzophenone hydrazones in acid solution, (2) to determine the rate of hydrolysis of p-methoxybenzophenone ketazine under the same conditions, and (3) to correlate these reactions as far as possible. The first work on hydrolysis rates of hydrazones was done by Johnson,³⁸ and the procedures which he developed for the study of the kinetics of these reactions were followed and applied as closely as possible to the study of the ketazines. Before attempting the main problem preliminary work was done in the study of the rates of hydrolysis of benzophenone hydrazone and benzophenone ketazine under similar conditions. The equations for these reactions are:



³⁸Johnson, loc. cit.

The Method of Procedure

The study of the rates of these reactions was based on the determination of the changing concentration of the hydrazine in the solution as the hydrolysis of the hydrazone or ketazine proceeded. An excellent method for the determination of hydrazine in acid solution has been worked out by Jamieson,³⁹ and carefully tested by Kolthoff.⁴⁰ This involves the titration of the hydrazine by means of standard potassium iodate solution in the presence of strong hydrochloric acid and a little chloroform to indicate the presence of free iodine. The end point is reached when the pink color of the iodine in the chloroform layer is just discharged. This method was used for this work. The titrations were carried out in glass stoppered Erlenmeyer flasks in which the substances could be thoroughly shaken.

The very limited solubility of these hydrazones and ketazines in hydrochloric acid solutions required the presence of an organic solvent in the hydrolyzing medium to obtain solutions of sufficient concentration for observation. Alcohol and other reducing solvents could not be employed as they would also react with the iodate in the subsequent titration of the hydrazine. The acetic acid-hydrochloric acid mixture as recommended by Johnson was found to be an excellent solvent. In most cases equal volumes of glacial acetic acid and standard hydrochloric acid were used. Careful tests showed that the presence of acetic acid did not interfere with the determination of the hydrazine by the potassium iodate in strong hydrochloric acid solution.

The weighed sample of the hydrazone was dissolved in pure glacial acetic acid at 25°C. in a volumetric flask and, as quickly as possible thereafter at observed time (T_0), a definite volume of standardized hydrochloric acid added. The volume was then made up to the mark using glacial acetic acid. The substances were thoroughly mixed and the reaction was permitted to proceed at 25°C. in a thermostat. At intervals (T_1, T_2, T_3 , etc.) aliquot samples were taken and the unchanged hydrazone and ketone extracted with four portions of chloroform in a separatory funnel. The aqueous layer was then transferred to a glass stoppered flask

³⁹Jamieson, Amer. Jour. Science, **33**, 352-53 (1912).

⁴⁰Kolthoff, J. Am. Chem. Soc., **46**, 2009 (1924).

and the hydrazine content estimated, using standardized KIO_3 solution. The details of the procedure may be found in the Experimental Part on page 25. The velocity coefficient, K, was calculated for a first order reaction using the following equation:

$$K = \frac{2.303}{T_1} \log \frac{A}{A - X_1}$$

In this equation (A) is the calculated volume (in cc.) of the standardized KIO_3 solution that would be required to titrate the hydrazine liberated on complete hydrolysis of the hydrazone contained in the aliquot portion of the hydrazone solution. X_1 is the volume of the standardized KIO_3 solution actually used to titrate the hydrazine liberated in the time interval T_1 (in minutes).

A number of runs on the hydrolysis of benzophenone hydrazone at different concentrations in the 50% acetic acid-hydrochloric acid medium gave values for K that demonstrate the merit of the procedure and confirm the apparent uni-molecular nature of the reaction as carried out.

No appreciable variation in the pH of the solution was detected during the hydrolysis or after 24 hours. Potentiometric measurements were made using the glass electrode (Coleman, Model 3-d, Coleman Electrical Company, Maywood, Illinois). The readings taken were also in accord with those taken at the same time on a similar solution of acetic acid-hydrochloric acid (but containing no hydrazine).

It was found that the molar solubilities of the ketazines were much less than that of the hydrazones. Tests of the solubility of p-methoxybenzophenone ketazine in the 50% acetic acid-hydrochloric acid medium showed that for concentrations not greater than 0.016 molar such a solvent would be satisfactory. However for the ketazine of benzophenone it was necessary to use a much more concentrated acetic acid solution to obtain sufficient solubility. For comparison of the rates of hydrolysis of benzophenone hydrazone and benzophenone ketazine 84% acetic acid-hydrochloric acid was used as a medium.

Ketazine formation

The formation of the ketazine was expected as an intermediate in the hydrolysis of the hydrazones or as a side reaction between two molecules of the ketone and one molecule of the hydra-

zine, produced during the hydrolysis of the hydrazones. It was hoped that this research might furnish some information on the part played by the ketazine in such reactions.

The method suggested by Chuang⁴¹ was found to give most satisfactory yields of benzophenone ketazine and p-methoxybenzophenone ketazine directly from the corresponding ketones. In this preparation the ketone is simply dissolved in glacial acetic acid, using a glass stoppered flask, and treated with slightly more than the theoretical amount of hydrazine hydrate and permitted to stand at room temperature for 3-4 days. The first appearance of ketazine crystals takes place within 24-36 hours. We were unable to obtain any indication of ketazine formation on heating benzophenone with the theoretical quantity of hydrazine hydrate in alcoholic solution, either under reflux or in a sealed tube at 150°C. for 6 hours. Practically quantitative yields of the hydrazones were obtained instead.

Shapiro⁴² reports the preparation of a number of ketazines by warming the ketone with hydrazine hydrochloride in 80% alcohol.

Johnson⁴³ observed the formation of the ketazine from benzophenone hydrazone when dilute alcoholic solutions were treated with equal volumes of 0.025 molar hydrochloric acid. Similar reactions were found to take place with either of the isomeric forms of p-methoxybenzophenone hydrazone. The same ketazine separates from such solutions, with yields of 60-70% after two days. If the concentration of the hydrochloric acid is increased to 0.2 molar there is no separation of the ketazine on standing, but the hydrolysis of the hydrazone proceeds to the formation of hydrazine hydrochloride and the ketone.

Solutions of p-methoxybenzophenone hydrazone (0.018 M.) in 50% acetic acid- 0.012 M (or less) hydrochloric acid were found to precipitate the ketazine on standing 2-3 hours. However the ketazine failed to precipitate when the hydrochloric acid was 0.018 molar or greater. The ketazines were removed by filtration after standing 25 hours. The yields were 10-30%. The mother liquors after the extraction of the dissolved ketazine with chloroform showed concentration of hydrazine 60-70% of that of the original hydrazone solutions.

⁴¹Chuang, loc. cit.

⁴²Schapiro, Ber., 62-B, 2133-36 (1929); Ibid., 66-B, 1103 (1933).

⁴³Johnson, loc. cit.

The ketazine of p-methoxybenzophenone separated with good yields from concentrated solutions of either the alpha or beta form of the hydrazone in pure glacial acetic acid.

Gilbert⁴⁴ evaluated the equilibrium constant and rate of hydrolysis of dimethyl ketazine in water solution at pH 4.95. He reports that he was able to prevent the formation of the ketazine from acetone and hydrazine hydrate by having the acid concentration 0.02 molar or greater.

Evidently the presence of small concentrations of acid favors the formation of ketazines. But it seems that this formation may be largely inhibited by stronger concentrations of acid.

Discussion of Results

Our investigations indicate that under similar conditions both forms of p-methoxybenzophenone hydrazone hydrolyze at the same rate to form the ketone and hydrazine in 50% acetic acid-hydrochloric acid solutions. The concentration of the hydrochloric acid was maintained high enough to repress largely the reverse action and at the same time inhibit to a great extent the formation of ketazine. Although slightly lower rates* were obtained for the hydrolysis of the ketazines under conditions as nearly identical as possible with those maintained during the hydrolysis of the hydrazones, it seems very likely that all these hydrolyses involve a similar mechanism. Some of the average rates from typical runs are given on the following page.

Since the experimentally determined rates of hydrolysis of the alpha and beta forms of p-methoxybenzophenone hydrazone and also that of the ketazine are so nearly the same, it seems logical to suppose that there may be some intermediate product common to the three reactions. If the rate of breakdown of this intermediate is then much slower than the other reactions involved, this rate would determine the rate of the three hydrolyses. Some confirmation of such an idea is gained from the similar agreement observed in the rates of hydrolysis of the hydrazones

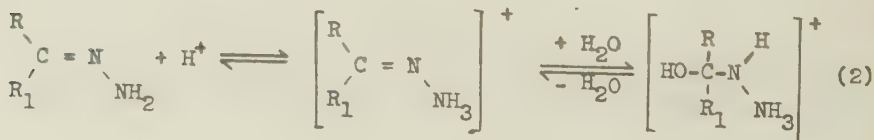
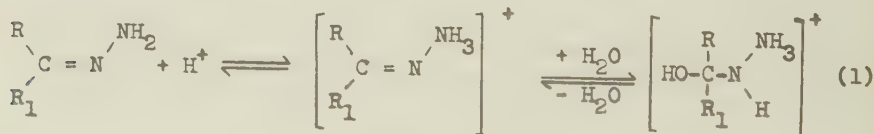
⁴⁴Gilbert, J. Am. Chem. Soc., 51, 3394 (1929).

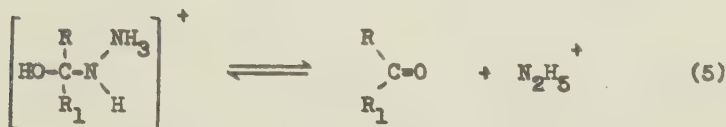
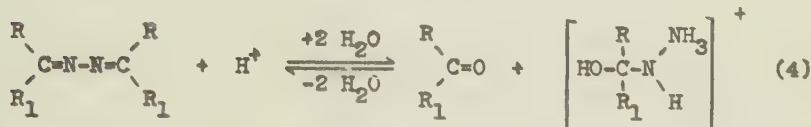
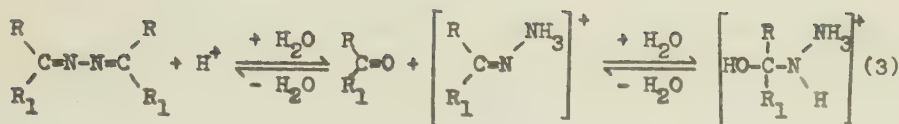
*The slightly lower rates for the ketazine might well be due to the fact that the ketazine was more efficiently extracted by the chloroform, e.g., the ketazine was practically quantitatively extracted by the first of the four extractions with chloroform.

AVERAGE RATES OF HYDROLYSIS
Temperature 25°C.

Compound	Molar Concent.	Mol. Conc. HCl	Per cent Hydrolyzed	Average K x 10 ⁴
alpha-p-Methoxybenzo- phenone Hydrazone	0.01414	0.4010	12.5-60.8	35.59
	0.01589	0.4010	15.5-60.5	34.62
	0.01512	0.4010	13.9-63.7	34.40
beta-p-Methoxybenzo- phenone Hydrazone	0.01522	0.4010	15.1-68.3	34.79
	0.01359	0.4010	16.5-65.7	34.14
	0.01573	0.4010	16.0-65.2	35.24
p-Methoxybenzophenone Ketazine	0.01525	0.4010	13.5-67.6	32.97
	0.01434	0.4010	14.0-67.5	33.12
	0.01405	0.4010	12.3-67.7	32.86
alpha-p-Methoxybenzo- phenone Hydrazone	0.01417	0.3391	14.8-63.2	29.12
	0.01357	0.3391	14.4-62.4	28.52
	0.01465	0.3391	13.7-62.8	28.75
beta-p-Methoxybenzo- phenone Hydrazone	0.01358	0.3391	14.1-62.4	29.04
	0.01449	0.3391	14.6-61.5	28.48
	0.01251	0.3391	14.6-62.6	29.39
p-Methoxybenzophenone Ketazine	0.01427	0.3391	12.0-60.7	26.36
	0.01328	0.3391	12.4-60.9	27.38
	0.01376	0.3391	12.7-64.7	26.88
Benzophenone Hydrazone	0.008788	0.5218	35.3-70.1	73.62
	0.008912	0.5218	34.1-73.9	71.90
Benzophenone Ketazine	0.008892	0.5218	32.9-76.4	70.05
	0.008935	0.5218	34.3-73.4	73.46
	0.008880	0.5218	15.8-75.4	70.67

and ketazine of benzophenone under similar conditions in 84% acetic acid-hydrochloric acid solution. To account for such intermediate and the reactions involved the following mechanisms are suggested:





If the three substances proceed rapidly in the presence of acid and water to the formation of the same intermediate ion as shown in equations (1) - (4) then a slow breakdown of this ion, equation (5), would determine the rate of the three overall reactions. Repeated attempts were made by extraction with chloroform to recover some of the hydrazone or other intermediate product from the partially hydrolyzed ketazine. The chloroform extract on evaporation gave only a yellow oil from which we were unable to recover any hydrazone.

The formation of the ketazine during the hydrolysis of the hydrazones might be accounted for from the reaction of the intermediate ion with ketone according to the reverse of equations (3) and (4). Although the concentration of the intermediate ion as postulated in equations (1) and (2) would be favored by acid solution and so promote ketazine formation, a large increase of the hydrogen ion concentration would favor the forward reactions in (3) and (4) and so prevent the formation of the ketazine.

The above mechanisms might suggest the existence of an equilibrium between the alpha and beta forms of the hydrazone through the formation of the same intermediate. However in the acid solution of the concentration used (0.4 N) this equilibrium would be greatly overshadowed by the hydrolysis to the ketone. And in weakly acid solution the reaction results in the formation of ketazine. The equilibria between the alpha and beta forms were not studied, but our investigations indicate that such studies would be very difficult in acid solution.

EXPERIMENTAL PART

A. The Preparation of Special Reagents

Benzophenone Hydrazone, $(C_6H_5)_2C=N-NH_2$

For the preparation of this compound a slight modification of the method described by Curtius and Rauterberg⁴⁵ was employed. A mixture of benzophenone (30.0 g. Eastman), hydrazine hydrate (10.8 g. Kahlbaum pure) and absolute alcohol (6.0 cc.) was heated in a sealed tube (encased in an iron pipe) at 150-155°C. for six hours in an oil bath. The tube was opened after cooling and the crude hydrazone was purified by two crystallizations from absolute alcohol. The benzophenone hydrazone appeared in long glistening white crystals. Melting point 98-99°C.; yield 31 grams.

Benzophenone Ketazine or Diphenyl Ketazine, $(C_6H_5)_2C=N-N=C(C_6H_5)_2$

An adaptation of the method suggested by Chuang⁴⁶ for the preparation of p-methylbenzophenone ketazine was found to be very direct, satisfactory, and economical for the preparation of diphenyl ketazine. A solution of benzophenone (7.5 g., Eastman) in glacial acetic acid (25 cc.) was treated with pure hydrazine hydrate (2.1 cc., Kahlbaum) and permitted to stand at room temperature in a glass stoppered flask. Crystals of the ketazine could usually be observed in the solution within twenty-four hours. At the end of four days the crystalline material was removed by filtration and washed with several small portions of alcohol. The crude, dried ketazine weighed 6.5 g. and showed a melting range of 155-158°C. The crystals were dissolved in warm chloroform (30.0 cc.) and the solution filtered into an Erlenmeyer flask. Ligroin (75 cc., boiling range 40-50°C.) was added to the solution, the flask was closed and left at room temperature for two days. A yield of 4.5 grams of almost colorless crystals,

⁴⁵Curtius and Rauterberg, J. prakt. Chemie, **44**, 194 (1891).

⁴⁶Chuang, loc. cit.

melting at 163°C., was obtained.

A method suggested by Johnson⁴⁷ for the preparation of the ketazine from the hydrazone was found to give satisfactory results. Benzophenone hydrazone (1.0 g., m.p. 98°C.) was dissolved in alcohol (60 cc., 95%) and treated with an equal volume of hydrochloric acid (approximately 0.03 N.). The solution turned yellow and within a few minutes a flocculent precipitate began to form. After the solution had stood over night the precipitate was removed by filtration and recrystallized from absolute alcohol. The diphenyl ketazine appeared in very pale yellow flakes having a melting point of 162-163°C. A mixture of these crystals and those prepared directly from the benzophenone melted at the same temperature, 162-163°C. The yield was 0.72 grams.

Attempts to prepare the ketazine in the absence of acid were unsuccessful. The two following methods gave negative results. Benzophenone (30.0 g., 1/6 mole), hydrazine hydrate ($\text{NH}_2\text{-NH}_2\text{,H}_2\text{O}$) (4.3 g., 1/12 mole) and absolute alcohol (7.0 cc.) were heated together in a sealed tube at 150-155°C. for seven hours. Two crystallizations of the product from alcohol gave 16.5 g. of benzophenone hydrazone, melting point 98-99°C. Ten grams of practically pure benzophenone were recovered from the filtrate from the first crystallization. The method suggested by Curtius and Rauterberg⁴⁸ for the preparation of the ketazine failed to give the expected results. A mixture of benzophenone hydrazone (9.8 g., 0.05 mole) and benzophenone (9.1 g., 0.05 mole) was heated in a small flask (connected with an air cooled condenser) at 150-155°C. in an oil bath for six hours. The mixture turned yellow showing some indication of ketazine formation, but, on recrystallization from alcohol, benzophenone hydrazone (7.6 g.) was obtained. No ketazine was recovered in either case.

p-Methoxybenzophenone, $\text{CH}_3\text{-O-C}_6\text{H}_4\text{-CO-C}_6\text{H}_5$

This reagent was prepared by the method described by Gattermann, Ehrhardt, and Maisch.⁴⁹ Benzoyl chloride (70 g.) was

⁴⁷Johnson, loc. cit.

⁴⁸Curtius and Rauterberg, loc. cit.

⁴⁹Gattermann, Ehrhardt, and Maisch. Ber., 23, 1204 (1890).

dissolved in freshly distilled carbon disulphide (600 cc.) in a one liter round-bottom flask. Anhydrous aluminum chloride (70 g.-reagent grade) was slowly added to this solution. The flask was then supported on a steam bath (in a well ventilated hood) and connected with a reflux condenser surmounted with a dropping funnel and delivery tube (to remove the HCl fumes). Anisole (50 g., Eastman) mixed with an equal volume of CS₂ was placed in the dropping funnel and admitted very slowly (approximately one hour being required) through the condenser tube into the reaction flask. The hydrogen chloride was evolved in a steady stream. The flask was agitated several times during the course of the reaction and heated somewhat with steam toward the end. After all the anisole had been added the funnel was replaced with a CaCl₂ drying tube and the mixture refluxed gently for three hours. The CS₂ was distilled off under diminished pressure, approximately 500 cc. being recovered in a receiver placed in an ice bath. Ice water (500 cc.) acidified with HCl was carefully added to the residue in the flask to hydrolyze the aluminum complex. The mixture in the flask was stirred vigorously and further cooled (using an ice bath) in order that the ketone would solidify in small lumps. The crude ketone was filtered off and the cool acid solution extracted with several portions of ether (900 cc. in all). The ether extract and the main portion of the ketone were combined and washed in a large separatory funnel with several portions of dilute NaOH, then with water and dried over CaCl₂. The ether solution was filtered from insoluble material and evaporated under diminished pressure to about half its volume. The ketone was then permitted to crystallize. Two or three recrystallizations from ether were required to give the pure p-methoxybenzophenone, m.p. 62°C. The average yield for six runs was about 75% of the theoretical.

The Stereoisomeric Hydrazones of p-Methoxybenzophenone,
 $\text{p-CH}_3\text{O-C}_6\text{H}_4\text{-C}=(\text{N-NH}_2)\text{-C}_6\text{H}_5$

A mixture of the two stereoisomeric compounds was prepared by a slight modification of the method of Stieglitz and Chuang.⁵⁰ The apparatus consisted of a three necked, one liter, round-bottom flask provided with an efficient mercury sealed mechanical stirrer and reflux condenser. The condenser was sur-

⁵⁰Chuang, loc. cit.

mounted with a CaCl_2 guard tube. The apparatus was supported in the hood on a steam bath in such a manner that the reagents could be introduced through the third opening in the flask. Barium oxide (28 g.-special grade from the J.H.R. Products Co., Willoughby, Ohio), absolute alcohol (25 cc.) and hydrazine hydrate (16 g.-Kahlbaum) were placed in the flask and the stirrer started. p-Methoxybenzophenone (40 g.) dissolved in 50 cc. of warm absolute alcohol was admitted into the reaction mixture by means of a dropping funnel. The mixture was vigorously stirred and gently heated so that the alcohol would slowly reflux for a period of 43-45 hours, usually covering a period of four days (daytime). The reaction mass was pale yellow in color, and solidified on cooling. At the end of the period the mixture was extracted with several portions of ether (using 350-400 cc. in all) and filtered from the barium hydroxide.

Using a slight change in the method suggested by Johnson⁵¹ a separation of the two isomers was accomplished without resorting to the picking out of unlike crystals. The ethereal solution as obtained above was transferred to a 500 cc. r.b. flask and most of the solvent removed under diminished pressure (approximately 300 mm. mercury), the flask being heated at 50°C. by means of warm water. When the ether had practically ceased to distill, the flask was closed and cooled in an ice bath for one hour. The crystals which formed in the flask were filtered off with suction and washed with a few cc. of ether. The pale yellow material when dry weighed 12.8 g. and showed a melting point range 78-81°C. A mixture of approximately equal amounts of this with the pure high melting isomer (m.p. 96°C.) showed a melting point range of 88-92°C. A similar mixture of the material with the low melting isomer (m.p. 86°C.) melted over a range of 68-71°C. Evidently the fraction was rich in alpha, or high melting isomer. This fraction was designated (A) and was purified as shown below. The ethereal filtrate from the above fraction was returned to the r.b. flask, using some ether, and the ether removed further as before with reduced pressure and water bath heated to 60°C. This when cooled in an ice bath for one hour yielded a fraction (B) of crystals weighing 6.2 g. with m.p. 80-83°C. Mixed melting point with the

⁵¹Johnson, loc. cit.

pure alpha form showed a range of 60-66°C., while a mixed melting point with the pure beta form or low melting isomer showed a range of 81-84°C. This fraction was evidently rich in the low melting form. Further fractions (C) of 6 grams m.p. 70-72 and (D) of 3.5 g., m.p. 60-65, were obtained from the ethereal solution on evaporating and chilling for longer periods. A final product of yellow oil (10 g.) that would not crystallize was obtained which has not been investigated further.

The (A) fraction (12.8 g.) was dissolved in approximately 25 cc. of warm purified xylene and filtered from a slight insoluble residue of $\text{Ba}(\text{OH})_2$ into 125 cc. Erlenmeyer flask (35 cc. of the xylene in all being used to dissolve and transfer to flask). To this was added 25 cc. of ligroin (b.p. 40-50°C.). After leaving to crystallize in closed flask at room temperature for 30 minutes, 8.5 g. of almost white crystalline solid was obtained, m.p. 92-94°C. This when recrystallized from 25 cc. of xylene, and 25 cc. of ligroin added, gave, on standing at room temperature for one hour, 6.5 g. of fine white crystals, m.p. 96°C.

The (B) fraction (6 g.) which had a deeper color was recrystallized once from ether yielding 4.8 g., melting at 82-84°C.; most of the color was removed. This on crystallizing once from xylene (15 cc.) and ligroin (15 cc.) gave 3.6 g. of pure beta hydrazone melting sharply at 86°C.

On further treatment with ligroin the mother liquors gave up practically all of the solid material. These samples were combined and further worked up in the manner indicated, yielding smaller portions of the pure forms. Mixed melting point determinations were frequently made from crystal fractions with the pure forms. This was of great assistance in determining which fractions to mix during the purifications. In the run just described, 9.2 g. of pure alpha form were obtained, and 4.3 g. of pure beta.

The high melting isomer was invariably obtained in the larger amount, and when pure appeared in fine white crystals (clusters). The beta or low melting isomer crystallized from the xylene-ligroin mixture in rhombic grains which were pale-green-glassy in appearance, and much more brittle than the alpha or high melting isomer. The pure beta when crushed gave a pure white powder. The melting range of approximately 50-50 mixtures of the two isomers was 60-65°C.

Residues of solid material, usually weighing 12-15 g. (m.p. 62-68°C.), of no definite crystalline shape were obtained on most runs. From this it was very difficult to obtain appreciable amounts of either of the pure forms.

p-Methoxybenzophenone Ketazine,
 $\text{p-CH}_3\text{O-C}_6\text{H}_4\text{-C-(C}_6\text{H}_5\text{)=N-N=C(C}_6\text{H}_5\text{)C}_6\text{H}_4\text{-OCH}_3$

The most satisfactory method found for the preparation of this compound was that of Chuang.⁵² p-Methoxybenzophenone (8 g.) was dissolved in glacial acetic acid (25 cc.) and treated with hydrazine hydrate (2.1 g.) and the solution left in a stoppered flask at room temperature for four days. The crystals obtained weighed 5.2 g., and melted at 132-133°C. The crude ketazine was dissolved in warm chloroform (25 cc.) and filtered into an Erlenmeyer flask. Ligroin (50 cc.-b.p. 40-50°C.) was added to the solution and the ketazine was permitted to crystallize in the closed flask for three days. A yield of 4.7 g. of the pure p-methoxybenzophenone ketazine, beautiful yellow clusters, melting sharply at 135°C., was obtained.

The ketazine was also prepared separately from each of the pure alpha and beta forms of the p-methoxybenzophenone hydrazone. Samples weighing 0.20 g. were dissolved (separately) in 15 cc. of warm alcohol. This gave clear colorless solutions. Each solution was cooled to room temperature and treated with 15 cc. of HCl approximately 0.03 N. The solutions turned yellow within a few minutes and developed a distinct cloudiness within 20-25 minutes. At the end of thirty hours the precipitates were filtered off and washed with small portions of alcohol. The crude ketazine from the beta form weighed 0.15 g. and melted within the range 131-133°C, while that from the alpha form weighed 0.14 g. and melted at 128-131°C. Each was recrystallized from chloroform (2 cc.) and ligroin (6 cc.). At the end of two days approximately 0.1 g. of ketazine was obtained from each. The melting point of each was 135°C. and a mixture of the two melted at the same temperature.

It was also found that the ketazine was formed from each of the hydrazones when they were dissolved in pure glacial acetic acid and the solution was permitted to stand for a number of hours. The pure alpha hydrazone (0.5 g.) was dissolved in glacial acetic

⁵²Chuang, loc. cit.

acid (1 cc.). Solution took place almost immediately and within ten minutes a distinct yellow color had developed. A slight crystallization of ketazine was apparent after standing one hour, and was much heavier after 4-5 hours. At the end of two days 0.39 grams of crystals were obtained melting at 131-133°C. On recrystallization from chloroform and ligroin as described above the pure ketazine (0.18 g.) was obtained. The pure beta form (0.3 g.) was dissolved in glacial acetic acid (0.7 cc.) with almost identical results. The solution turned yellow within ten minutes and crystals were apparent after forty minutes. At the end of two days crude ketazine weighing 0.22 g. and melting at 131-133°C. was obtained. Recrystallization from chloroform-ligroin mixture gave 0.15 g. of pure ketazine.

A number of tests for ketazine formation were made on samples of alpha-p-methoxybenzophenone hydrazone dissolved in 50% acetic acid but containing different concentrations of hydrochloric acid. Equal weights (0.400 g.) of the hydrazone were dissolved as quickly as possible in pure glacial acetic acid (50.0 cc.) at room temperature using Erlenmeyer flasks. Dilute hydrochloric acid (50.0 cc. of different concentrations) was added to the dissolved samples at as nearly the same time as possible. The concentrations of the hydrochloric acid added to the six samples varied from zero to 0.036 N. Each solution immediately became bright yellow, the color characteristic of the ketazine, but there was no indication of precipitate in any of the flasks for two hours. After three hours there were pronounced precipitates in all the flasks except the one containing the strongest concentration of hydrochloric acid (in which no precipitation occurred at any time). The yellow ketazine precipitates became heavier on standing and were recovered by filtration after 25-26 hours. Samples (25.01 cc.) of the mother liquors were taken, diluted with water (50 cc.) and extracted with four portions of chloroform (8-6-6-6 cc.) to remove the dissolved ketazine and unchanged hydrazone and the aqueous layer analyzed for the hydrazine content using KIO_3 solution (0.0183 molar). The table on the following page gives a brief summary of the results.

The calculated volume of the standardized KIO_3 solution required to titrate the hydrazine formed on complete hydrolysis of the hydrazone contained in 25.01 cc. of the original samples is 24.18 cc.

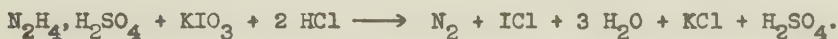
In each case the mother liquors lost all color on standing 24-48 hours longer.

Sample Number	Molar Conc. of HCl in Solution	Precipit. Appeared on Standing Minutes	Grams of Ketazine Recovered After 25 Hours	Volume cc. 0.0183 M KIO ₃ Required for 25.01 cc. After 25 Hours
1	0.000	130	0.11	15.39
2	0.002	130	0.14	14.75
3	0.004	120	0.09	15.03
4	0.008	180	0.04	15.58
5	0.012	150	0.03	17.45
6	0.018	...	0.00	18.21

From the above tests it seems fair to assume that the ketazine formation was negligible in the hydrazone solutions used for our rate of hydrolysis determinations where the concentration of hydrochloric acid was 0.34 to 0.52 normal.

The Standardization of Potassium Iodate Solution

It was shown by Jamieson⁵³ and further verified by Kolthoff⁵⁴ that KIO₃ reacts smoothly and quantitatively at room temperatures with hydrazine sulphate in water solution in the presence of strong HCl according to the following equation:



Small amounts of CHCl₃ or CCl₄ were recommended as indicators to detect when sufficient KIO₃ had been added to oxidize the free iodine which is first formed to ICl. The method of these investigators was used in the standardization of the potassium iodate solutions (approximately 0.018 molar) to be used later in the estimation of hydrazine.

The KIO₃ used for the preparation of the solutions was Reagent Grade which had been twice recrystallized from water and dried over concentrated sulphuric acid. In one case a sample of the salt (15.42 g., KIO₃) was dissolved in water, made up to 4 liters, thoroughly mixed and permitted to stand 24 hours before standardizing. The hydrazine sulphate, to be used as a primary

⁵³Jamieson, Amer. Jour. Science, **33**, 352-53 (1912).

⁵⁴Kolthoff, J. Am. Chem. Soc., **46**, 2009 (1924).

standard, was prepared by recrystallizing the Eastman reagent twice from water and drying at 140°C. for one hour. The salt was preserved in a vacuum desiccator prior to use. Carefully weighed samples (50-70 mg.) were placed in 250 cc. glass stoppered Erlenmeyer flasks and dissolved in measured volumes of water (60 cc.). Hydrochloric acid (30.0 cc., C.P., sp. gr., 1.19) and chloroform (6 cc.) were added to each flask just prior to titration. The KIO_3 solution was run in slowly with agitation. As the end point was approached the flask was stoppered and shaken vigorously between the addition of each drop and the chloroform permitted to settle. The end point was taken when the pink color was just discharged from the chloroform layer.

Weight g. $\text{N}_2\text{H}_4\cdot\text{H}_2\text{SO}_4$	Volume, cc. KIO_3 Solut.	Wt. Sample g. cc. KIO_3 Used *
0.0641	27.10	0.002365
0.0500	21.11	0.002369
0.0470	19.94	0.002359
Average titre		0.002365 (No Acetic Acid Used)

It was shown by the following titrations that glacial acetic acid, in the concentrations as noted, does not interfere with the standardization of the KIO_3 solution or with the estimation of hydrazine under such conditions. Samples of the hydrazine sulphate were weighed into the glass stoppered Erlenmeyer flasks just as in the previous case. The samples were dissolved using 47.5 cc. of water in each case and 12.5 cc. of glacial acetic acid added. Hydrochloric acid (30.0 cc., C.P., sp.gr.,1.19) and chloroform (6 cc.) were added and the titration with the KIO_3 solution carried out exactly as before.

Weight g. $\text{N}_2\text{H}_4\cdot\text{H}_2\text{SO}_4$	Volume cc. KIO_3 Solut.	Wt. Sample g. cc. KIO_3 Used
0.0485	20.46	0.002376
0.0520	21.77	0.002389
0.0507	21.29	0.002381
Average titre		0.002382 (Acetic Acid Used)

*In all this research Class S standardized weights were employed. Pipettes were standardized by determining the weight of water delivered when permitted to drain 30 secs. The pipette when used was always permitted to drain the same length of time. Burettes were standardized by determining the weight of water delivered, and volumetric flasks were calibrated by the weight of water contained at 25°C.

Since glacial acetic acid was to be present when estimating the hydrazine in solution resulting from the hydrolysis of the hydrazone, it was added here in the amount noted and the molarity of the KIO_3 solution calculated from the titre found in that case:

$$\begin{aligned}\text{Molarity KIO}_3 \text{ Sol.} &= \frac{\text{Titre} \times 1000}{\text{Mol. Wt. N}_2\text{H}_4 \cdot \text{H}_2\text{SO}_4} \\ &= \frac{0.002382 \times 1000}{130.12} \\ &= 0.0183_1.\end{aligned}$$

B. The Determination of Hydrolysis Rates

Rate of Hydrolysis of Benzophenone Hydrazone

Preliminary to later investigations, and in order to become familiar with the technique involved, the rate of hydrolysis of benzophenone hydrazone as reported by Johnson⁵⁵ was determined. Many of these details will not be discussed here except to state that his findings were verified.

The procedure given was carefully observed. An accurately weighed sample of benzophenone hydrazone was quantitatively transferred to a 500 cc. volumetric flask, and dissolved as rapidly as possible in 235 cc. of pure glacial acetic acid at exactly 25°C. At a carefully noted time (T_0) hydrochloric acid 0.8019 N* (exactly 250.0 cc. at temperature 25°C.) was added. The volume of the solution was made up as quickly as possible to 500.0 cc. by addition of acetic acid and the solution thoroughly mixed. The solution was then transferred to a 500 cc. round-bottom flask and placed in a thermostat held at $25.00 \pm 0.02^\circ\text{C}$. The flask was

⁵⁵Johnson, loc. cit.

*The hydrochloric acid was standardized against weighed samples of anhydrous sodium carbonate of known purity, using methyl orange as indicator. Before use the Na_2CO_3 was dried for one hour at 140°C. and kept in vacuum desiccator.

The quality of the glacial acetic acid used was found to have a great effect on the values obtained for K in different runs. The C.P. grades from different sources would not give concordant results. Further purification of the C.P. acid by the method of Echelberger and La Mer (J. Am. Chem. Soc., 55, 3633 [1933]), was found to yield a uniform product for our work.

closed with a gum stopper through which was passed the stem of a calibrated pipette reaching almost to the bottom of the flask. Aliquot portions (25.01 cc.) of the solution were removed at intervals and transferred to a 125 cc. separatory funnel and 25 cc. of water at 25°C. added. The solution was then extracted with four successive portions of chloroform (8-6-6-6 cc.) at exactly two minute intervals. The chloroform was vigorously shaken with the solution each time, permitted to settle for one and one-half minutes and then withdrawn from the funnel (the stem of which had been ground off diagonally close to the stopcock). The stem was rinsed after the last portion of chloroform had been withdrawn and the sample containing the hydrazine transferred to a 250 cc. glass stoppered Erlenmeyer flask, using 10 cc. of water to rinse the funnel. Chloroform (6 cc.) to act as an indicator and hydrochloric acid (30 cc., C.P., sp.gr., 1.19) were added and the titration with the standardized KIO_3 solution carried out at once. The time interval (T_1, T_2, T_3 etc.) for each sample was taken from the time of mixing (T_0) until the third portion of chloroform was added to the sample. The values of K, the velocity constant, as expressed in the differential equation for a first order reaction,

$$\frac{dx}{dt} = K(A - X),$$

were obtained by using the integrated form

$$K = \frac{2.303}{T_1} \log_{10} \frac{A}{(A - X_1)}.$$

In this equation (A) is the calculated volume (in cc.) of the standardized KIO_3 solution required to titrate the hydrazine that would be liberated on complete hydrolysis of the hydrazine contained in the 25.01 cc. sample taken from the reaction flask. X_1 is the volume (in cc.) actually used to titrate the hydrazine liberated in the time interval T_1 .

On a representative run (A) was calculated as follows:

Weight of benzophenone hydrazone	1.8002 g.
Dissolved and made up to	500.0 cc.

$$\text{Molarity of solution} = \frac{1.8002 \times 2}{196.09} = 0.0183_6$$

Volume of sample taken	25.01 cc.
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Molarity of KIO_3 solution	0.0181_6
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$$A = \frac{0.01836 \times 25.01}{0.01816} = 25.29 \text{ cc.}$$

The data on two representative runs are summarized in Tables 1 and 2 below.

Hydrolysis Rates of Benzophenone Hydrazone

Solvent 50% Acetic Acid, HCl 0.4010 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01816 M.

TABLE 1

Molarity of Hydrazone 0.0183₆. A = 25.29

T	X	A - X	% Hydrol.	$K \times 10^4$
23	2.83	22.46	11.19	51.54
56	6.80	18.49	26.89	55.89
88	9.84	15.45	38.92	55.98
121	12.34	12.95	48.80	55.31
161	14.88	10.41	58.85	55.12
199	16.00	9.29	62.28	50.21
240	17.61	7.68	69.64	49.65
Average $K = 53.39 \times 10^{-4}$				

TABLE 2

Molarity of Hydrazone 0.0174₅. A = 24.03

T	X	A - X	% Hydrol.	$K \times 10^{-4}$
24	2.82	21.21	11.74	52.01
56	6.49	17.54	27.01	56.22
91	9.61	14.42	39.99	56.13
122	11.83	12.20	49.23	55.57
160	14.12	9.91	58.76	55.37
198	15.38	8.65	64.00	51.61
240	16.65	7.38	69.29	49.20
Average $K = 53.73 \times 10^{-4}$				

The Hydrolysis Rates of Benzophenone Hydrazone and Benzophenone Ketazine Under Similar Conditions

The rate of solubility of benzophenone ketazine in pure glacial acetic acid is very slow at room temperature. A sample of the ketazine (0.10 g.) failed to dissolve completely in 25 cc. of glacial acetic acid with shaking at frequent intervals over a period of four hours. With smaller amounts of the acetic acid the ketazine (0.10 g.) dissolved on gently warming on a steam bath but would recrystallize on cooling. A volume of at least 20 cc. of acetic acid was required to keep the sample (0.10 g.) in solution on cooling to room temperatures. A sample (0.10 g.) of the ketazine was dissolved in 25 cc. of warm glacial acetic acid and cooled to room temperature. To this solution hydrochloric acid (approximately 0.80 molar) was added from a burette, slowly with shaking. A precipitate persisted after adding 13 cc. of the HCl. This very limited solubility of the ketazine in the glacial acetic-hydrochloric acid medium necessitated a change to a solvent stronger than 50% acetic acid. It was not thought practical to attempt to estimate the rate of hydrolysis of the ketazine (mol.wt.360) by the method described in solutions much less concentrated than 0.01 molar with respect to the ketazine. A solution of 0.10 g. of ketazine in 25 cc. of acetic acid was found to remain clear on shaking with 5 cc. of 2.5 molar HCl. This seemed to be about the best concentration that might be realized.

The procedure adopted for estimating the rate of hydrolysis in such concentrations was as follows. A sample of the ketazine (near 0.8 g.) weighed accurately was dissolved in 180 cc. of highly purified, warm acetic acid and cooled to room temperature. The solution was then transferred carefully to a calibrated 250 cc. volumetric flask, using 20 cc. of acetic acid to make the transfer (200 cc. in all being used). The flask was closed and placed in a thermostat, held at $25 \pm 0.02^{\circ}\text{C}$., for thirty minutes. At a definite time (T_0) hydrochloric acid (40.00 cc., 2.609 molar at 25°C .) was added as rapidly as possible with shaking, and the flask filled to the mark with glacial acetic acid. After a thorough mixing the solution was transferred to a 300 cc. round-bottom flask and placed in a thermostat kept at $25 \pm 0.02^{\circ}\text{C}$. At intervals of 20-25 minutes samples (25.01 cc.) were removed and analyzed for the hydrazine content as follows. Each sample was

placed in a 125 cc. separatory funnel, diluted with 50 cc. of water at 25°C. and extracted with four portions of chloroform (8-6-6-6 cc.) at intervals of exactly two minutes. After the removal of the last portion of chloroform, the stem of the funnel was rinsed and the sample was transferred to a 250 cc., g.s., Erlenmeyer flask using 10 cc. of water to rinse the funnel. Hydrochloric acid (45 cc., C.P., sp.gr., 1.19) and chloroform (6 cc.) were added and the titration of the hydrazine completed with 0.0181₆ molar KIO₃ solution. The time interval (T_1) was taken from the time of mixing the solution (T_0) to the addition of the third portion of chloroform for the extraction of the ketazine. The values A, X, and K have the same significance as in the previous runs on the hydrazone. The calculations were carried out in the same manner.

The rate of hydrolysis of benzophenone hydrazone was also investigated under these conditions. The weighed sample of the hydrazone was transferred to a 250 cc. volumetric flask and dissolved using 200 cc. of glacial acetic acid at 25°C. (no heating being necessary). At the definite time (T_0) HCl (40.00 cc., 2.609 molar at 25°C.) was added and the volume made up to the mark as rapidly as possible. The procedure from this point was identical with that given above.

The use of the 84% acetic acid as a solvent in these runs was found to necessitate the slight changes as shown above in extracting the unchanged ketazine and hydrazone from the samples. The significant change in the procedure here from that used in earlier runs was the addition of 50 cc. of water (instead of 25 cc.) to the sample taken from the reaction flask before the extraction with chloroform. A number of runs were made where the original conditions were followed (adding 25 cc. of water). Erratic results were obtained, especially in the case of the hydrazone. Definite end points were very hard to establish in the titration of the hydrazine from each sample: the color of iodine when once discharged would return to the chloroform layer within 15-25 seconds and on standing would be very pronounced. It seemed evident that the unhydrolyzed hydrazone or ketazine was not being effectively extracted before the titration. The addition of 50 cc. of water instead of 25 cc. brought the acetic acid-water ratio in the sample to be extracted to approximately the same value as in the original conditions. With the conditions as reported the end

points in the titrations were much sharper and the calculated values for K more satisfactory. Before the titration the concentration of HCl was adjusted by the addition of 45 cc. of the concentrated HCl instead of 30 cc. as used previously.

The data on some of the representative runs are given below in Tables 3 to 7. The results are not as concordant as desired but seem to be as close as may be expected considering the high dilution and other limitations.

Hydrolysis Rates of Benzophenone Hydrazone

Solvent 84% Acetic Acid, HCl 0.5218 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01816 M.

TABLE 3

Molarity of Hydrazone 0.008788. A = 12.10

T	X	A - X	% Hydrol.	K x 10^4
58	4.28	7.82	35.37	75.32
80	5.64	6.46	46.61	78.47
99	6.67	5.43	51.12	(80.22)
118	7.10	5.00	58.68	74.93
139	7.85	4.25	64.87	75.31
157	8.33	3.77	68.81	74.14
177	8.59	3.51	70.99	70.60
197	8.84	3.26	73.06	66.60

Average K = 73.62×10^{-4}

TABLE 4

Molarity of Hydrazone 0.008912. A = 12.27

T	X	A - X	% Hydrol.	K x 10^4
57	4.19	8.08	34.15	73.38
78	5.48	6.79	44.66	75.91
100	6.54	5.73	53.30	76.23
120	7.30	4.97	59.49	75.35
142	7.84	4.43	63.90	73.21
162	8.39	3.88	68.38	71.10
188	8.76	3.51	71.39	66.60
212	9.07	3.20	73.92	63.42

Average K = 71.90×10^{-4}

Hydrolysis Rates of Benzophenone Ketazine

Solvent 84% Acetic Acid, HCl 0.5218 N₂
 Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
 Volume of Sample 25.01 cc.
 A and X in cc. of KIO₃ 0.01816 M.

TABLE 5

Molarity of Ketazine 0.008892. A = 12.25

T	X	A - X	% Hydrol.	K x 10 ⁴
59	4.04	8.21	32.98	(67.76)
80	5.38	6.87	43.92	72.25
102	6.45	5.80	52.65	73.29
122	7.16	5.09	58.45	71.98
143	7.79	4.46	63.59	70.70
166	8.42	3.83	68.73	70.04
188	8.83	3.42	72.08	67.87
213	9.13	3.12	74.53	64.20
237	9.37	2.88	76.49	(61.08)

Average K = 70.05×10^{-4}

TABLE 6

Molarity of Ketazine 0.008935. A = 12.31

T	X	A - X	% Hydrol.	K x 10 ⁴
57	4.23	8.08	34.36	73.82
77	5.37	6.94	43.62	74.38
97	6.39	5.92	51.91	75.45
117	7.20	5.11	58.49	75.13
138	7.86	4.45	63.85	73.70
160	8.42	3.89	68.40	71.98
180	8.75	3.56	71.08	68.91
206	9.04	3.27	73.44	64.34

Average K = 73.46×10^{-4}

TABLE 7

Molarity of Ketazine 0.008880. A = 12.23

T	X	A - X	% Hydrol.	K x 10 ⁴
30	1.94	10.29	(15.86)	(57.57)
59	4.16	8.07	34.01	70.48
82	5.54	6.69	45.30	73.58
109	6.84	5.39	55.93	75.17
145	7.86	4.37	64.27	70.98
170	8.43	3.80	68.93	68.76
216	9.23	3.00	75.47	65.07

Average K = 70.67×10^{-4}

The Hydrolysis Rates of p-Methoxybenzophenone Ketazine and the Isomeric p-Methoxybenzophenone Hydrazones under Similar Conditions

It was expected that the solubility of the p-methoxybenzophenone ketazine would be a limiting factor in determining the hydrolysis rates of this compound and that of the isomeric p-methoxybenzophenone hydrazones in the 50% acetic acid-hydrochloric acid medium. The solubility of the ketazine was investigated. The substance was very slow to dissolve in glacial acetic acid, but on warming dissolved readily. When small portions of the acid were used the ketazine recrystallized on cooling to room temperature. Two samples, each weighing 0.15 g., of the ketazine were dissolved, using 50 cc. Erlenmeyer flasks, by warming in 10 cc. of glacial acetic acid. The ketazine remained in solution when the solution was cooled to 25°C. To each solution hydrochloric acid (0.6 molar) was added slowly from a burette. On the addition of a few drops of the acid a yellow precipitate appeared, but dissolved almost immediately when the flask was shaken. The solutions were watched carefully between additions of the acid. In one case the solution showed evidence of a permanent precipitate when 12.2 cc. of the HCl had been added and in the other when 12.4 cc. had been added. This indicated that solutions of the ketazine (m.w. 420.21) approximately 0.015 molar might be prepared in 50% acetic acid-hydrochloric acid medium for the studies of the hydrolysis rates. Both forms of the p-methoxybenzophenone hydrazones showed much higher solubilities than the ketazine.

The hydrolysis of each of the three compounds was investigated under carefully controlled conditions in the 50% glacial acetic acid solution. In one series of runs the concentration of the hydrochloric acid was 0.401₀ molar and in the other 0.339₁ molar.

In the case of the hydrazones the procedure was identical as far as possible with that of the benzophenone hydrazone described on page 25. The p-methoxybenzophenone hydrazone was in a finely divided condition and dissolved very rapidly in the pure acetic acid (at exactly 25°C.). With shaking this could be done in less than one minute, minimizing as far as possible the formation of any ketazine. The hydrochloric acid solution was then

added quickly through a wide funnel while the volumetric flask was whirled. The flask containing the HCl was rinsed twice with small portions of glacial acetic acid into the main solution and the volume made up to the mark with the acetic acid. The solution was thoroughly mixed, transferred to a round-bottom flask and placed in thermostat held at $25 \pm 0.02^{\circ}\text{C}$.

For the ketazine the acetic acid was warmed to $60-70^{\circ}$ in order to effect solution. The solution was then cooled to room temperature, transferred to volumetric flask using several portions of acetic acid as a rinse, and placed in thermostat at $25 \pm 0.02^{\circ}\text{C}$. for at least thirty minutes before adding the HCl solution and making up to the standard volume.

In each case at intervals of approximately 40 minutes aliquot portions (25.01 cc.) were transferred to a 125 cc. separatory funnel and 50 cc. of water at 25°C . added. The unchanged hydrazone or ketazine was immediately extracted using four portions of chloroform (8-6-6-6 cc.) at exactly two minute intervals. When the last portion of chloroform had been withdrawn the short stem of the funnel was rinsed with water and the sample containing the hydrazine transferred to a 250 cc., g.s., Erlenmeyer flask (using 10 cc. of water to rinse the funnel). The chloroform indicator (6 cc.) and 45 cc. of concentrated HCl were then added and the hydrazine immediately titrated with the standardized KIO_3 solution.* The end point was taken when the last trace of pink color was discharged from the chloroform layer and so remained on shaking for at least one minute. The time interval for each sample (T_1, T_2, T_3 etc.) was taken as before from the time of mixing the HCl with the hydrazone solution (T_0) until the third sample of chloroform was added to the sample for extracting the unchanged hydrazone. The factors (A) and (A - X) have the same significance as in the previous investigations.

A number of runs were made on each compound in the two media. The following tables 8 - 25 give the data obtained on some

*In the titration of the hydrazine in samples from which the unchanged hydrazone or ketazine had been extracted with chloroform, it was found most satisfactory to admit the KIO_3 solution rather rapidly into the strong HCl-chloroform mixture. When the iodate had been admitted to within one or two cc. of the expected volume the flask was closed and vigorously agitated. The end point was then approached carefully. The titration was carried out within 6 minutes from the time of adding the first KIO_3 solution. The end point was taken when the chloroform layer would remain colorless for one minute.

of the representative runs. K is calculated for a first order reaction.

Hydrolysis Rates of alpha-p-Methoxybenzophenone Hydrazone

Solvent 50% Acetic Acid, HCl 0.4010 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 8

Molarity of Hydrazone 0.01414. A = 19.31

T	X	A - X	% Hydrol.	$K \times 10^4$
39	2.42	16.89	12.53	34.34
67	4.14	15.17	21.44	36.02
100	5.89	13.42	30.50	36.38
147	7.91	11.40	40.96	35.86
183	9.46	9.85	48.99	36.78
220	10.46	8.85	54.17	35.48
269	11.73	7.58	60.75	34.77
Average K = 35.59×10^{-4}				

TABLE 9

Molarity of Hydrazone 0.01589. A = 21.72

T	X	A - X	% Hydrol.	$K \times 10^4$
44	3.37	18.34	15.52	38.35
74	5.21	16.50	23.99	37.10
114	7.19	14.52	33.10	35.29
155	8.90	12.81	40.97	34.04
194	10.33	11.38	47.56	33.30
231	11.70	10.01	53.87	33.52
302	13.14	8.57	60.50	30.78
Average K = 34.62×10^{-4}				

TABLE 10

Molarity of Hydrazone 0.01512. A = 20.66

T	X	A - X	% Hydrol.	$K \times 10^4$
43	2.87	17.79	13.89	34.80
82	5.31	15.35	25.70	36.22
116	6.92	13.74	33.50	35.10
156	8.60	12.06	41.63	34.52
192	10.21	10.45	49.42	35.50
235	11.27	9.39	54.55	33.56
280	12.14	8.52	58.76	31.64
322	13.16	7.50	63.70	31.48
Average K = 34.30×10^{-4}				

Hydrolysis Rates of beta-p-Methoxybenzophenone Hydrazone

Solvent 50% Acetic Acid, HCl 0.4010 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 11

Molarity of Hydrazone 0.01522. A = 20.80

T	X	A - X	% Hydrol.	$K \times 10^4$
45.0	3.15	17.65	15.14	36.44
85.2	5.51	15.29	26.49	36.11
127.0	7.36	13.44	35.39	35.37
169.0	9.13	11.67	43.90	35.04
206.0	10.37	10.43	49.86	33.51
250.0	11.79	9.01	56.68	33.47
290.0	13.01	7.79	62.55	33.88
326.5	14.20	6.60	68.27	35.16

Average $K = 34.79 \times 10^{-4}$

TABLE 12

Molarity of Hydrazone 0.01359. A = 18.56

T	X	A - X	% Hydrol.	$K \times 10^4$
49.5	3.06	15.50	16.49	36.42
87.5	5.10	13.46	27.48	36.74
130.0	6.85	11.71	36.91	35.43
171.0	8.31	10.25	44.78	34.70
211.0	9.68	8.88	52.16	34.91
251.0	10.57	7.99	56.95	33.59
281.0	11.14	7.42	60.02	32.64
310.0	11.62	6.94	62.61	31.74
337.0	12.20	6.36	65.73	31.07

Average $K = 34.13 \times 10^{-4}$

TABLE 13

Molarity of Hydrazone 0.01573. A = 21.49

T	X	A - X	% Hydrol	$K \times 10^4$
47.0	3.45	18.04	16.05	37.27
79.0	5.54	15.95	25.78	37.75
116.0	7.67	13.82	35.69	38.04
158.0	9.26	12.23	43.09	36.19
196.0	10.52	10.97	48.95	34.32
232.0	11.70	9.79	54.44	33.90
270.0	12.92	8.57	60.12	34.06
302.0	13.78	7.71	64.12	33.96
334.0	14.01	7.48	65.19	31.68

Average $K = 35.24 \times 10^{-4}$

Hydrolysis Rates of p-Methoxybenzophenone Ketazine

Solvent 50% Acetic Acid, HCl 0.4010 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 14
Molarity of Ketazine 0.01525. A = 20.83

T	X	A - X	% Hydrol.	$K \times 10^4$
52	2.82	18.01	13.54	(28.02)
88	4.61	16.22	22.13	31.06
128	7.08	13.75	33.99	32.48
172	9.35	11.48	44.89	34.65
204	10.46	10.37	50.22	34.21
243	11.28	9.55	54.15	32.11
281	12.35	8.48	59.29	32.00
310	13.56	7.27	65.10	33.97
339	14.09	6.74	67.64	33.30
Average $K = 32.97 \times 10^{-4}$				

TABLE 15
Molarity of Ketazine 0.01434. A = 19.60

T	X	A - X	% Hydrol.	$K \times 10^4$
52	2.72	16.88	13.98	(28.71)
91	4.89	14.71	24.95	31.53
129	6.66	12.94	33.98	32.19
171	8.73	10.87	44.54	34.48
202	9.87	9.73	50.36	34.65
238	10.97	8.63	55.97	34.47
275	11.68	7.92	59.59	32.95
312	12.36	7.24	63.06	31.93
342	13.22	6.38	67.45	32.82
Average $K = 33.12 \times 10^{-4}$				

TABLE 16
Molarity of Ketazine 0.01405. A = 19.20

T	X	A - X	% Hydrol.	$K \times 10^4$
48	2.37	16.83	12.34	(27.41)
86	4.54	14.66	23.65	31.39
119	6.14	13.06	31.98	32.40
163	8.00	11.20	41.67	33.08
206	9.39	9.81	48.91	32.60
246	10.78	8.42	56.15	33.51
278	11.53	7.67	60.05	33.01
306	12.31	6.89	64.11	33.50
333	12.99	6.21	67.66	33.90
Average $K = 32.86 \times 10^{-4}$				

Hydrolysis Rates of alpha-p-Methoxybenzophenone Hydrazone

Solvent 50% Acetic Acid, HCl 0.03391 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 17

Molarity of Hydrazone 0.01417. A = 19.37

T	X	A - X	% Hydrol.	K x 10 ⁴
52	2.87	16.50	14.81	30.83
97	4.77	14.60	24.63	29.16
140	6.70	12.67	34.59	30.31
184	8.20	11.17	42.33	29.93
231	9.42	9.95	48.63	28.84
273	10.37	9.00	53.54	28.08
317	11.43	7.94	59.01	28.14
363	12.25	7.12	63.24	27.70

Average K = 29.12×10^{-4}

TABLE 18

Molarity of Hydrazone 0.01357. A = 18.54

T	X	A - X	% Hydrol.	K x 10 ⁴
57	2.67	15.87	14.40	27.30
100	4.61	13.93	24.86	28.60
147	6.37	12.17	34.36	28.65
184	7.69	10.85	41.48	29.02
224	8.71	9.83	46.98	28.34
262	9.72	8.82	52.43	28.31
302	10.83	7.71	58.41	29.06
338	11.56	6.98	62.35	28.91

Average K = 28.52×10^{-4}

TABLE 19

Molarity of Hydrazone 0.01465. A = 20.02

T	X	A - X	% Hydrol.	K x 10 ⁴
54	2.75	17.27	13.74	27.31
95	4.78	15.24	23.88	28.68
142	6.75	13.27	33.72	28.95
180	8.29	11.73	41.36	29.68
224	9.72	10.30	48.55	29.66
268	10.72	9.30	52.33	28.61
313	11.80	8.22	58.94	28.40
345	12.58	7.44	62.84	28.69

Average K = 28.75×10^{-4}

Hydrolysis Rates of beta-p-Methoxybenzophenone Hydrazone

Solvent 50% Acetic Acid, HCl 0.3391 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 20

Molarity of Hydrazone 0.01358. A = 18.55

T	X	A - X	% Hydrol.	$K \times 10^4$
55	2.61	15.94	14.07	27.58
100	4.73	13.82	20.25	29.45
138	6.22	12.33	33.53	29.61
179	7.52	11.03	40.54	29.05
216	8.76	9.79	47.22	29.87
256	9.72	8.83	52.40	29.01
301	10.92	7.63	58.87	29.52
347	11.58	6.97	62.43	28.22

Average $K = 29.04 \times 10^{-4}$

TABLE 21

Molarity of Hydrazone 0.01449. A = 19.79

T	X	A - X	% Hydrol.	$K \times 10^4$
55	2.89	16.90	14.60	28.74
98	4.84	14.95	24.46	28.65
135	6.62	13.17	33.45	30.18
174	7.81	11.98	39.46	28.87
222	9.06	10.73	45.78	27.59
264	10.19	9.60	51.49	27.42
300	11.34	8.45	57.30	28.38
346	12.17	7.52	61.50	27.98

Average $K = 28.48 \times 10^{-4}$

TABLE 22

Molarity of Hydrazone 0.01251. A = 17.10

T	X	A - X	% Hydrol.	$K \times 10^4$
55	2.51	14.59	14.58	28.85
99	4.40	12.70	20.45	30.03
138	5.82	11.28	34.03	30.16
172	6.99	10.11	40.88	30.55
217	8.02	9.08	46.90	29.19
251	8.83	8.27	51.64	28.95
297	9.84	7.26	57.62	28.85
344	10.70	6.40	62.57	28.57

Average $K = 29.39 \times 10^{-4}$

Hydrolysis Rates of p-Methoxybenzophenone Ketazine

Solvent 50% Acetic Acid, HCl 0.3391 N.
Time (T) in Minutes; Temp. $25 \pm 0.02^\circ\text{C}$.
Volume of Sample 25.01 cc.
A and X in cc. of KIO_3 0.01831 M.

TABLE 23

Molarity of Ketazine 0.01427. A = 19.45

T	X	A - X	% Hydrol.	K x 10 ⁴
59	2.34	17.11	12.03	(22.10)
101	4.45	15.00	22.88	25.81
151	6.33	13.12	32.54	26.22
186	7.49	11.96	38.51	26.26
226	8.72	10.73	44.83	26.41
268	9.96	9.49	51.21	26.86
314	10.99	8.46	56.50	26.59
357	11.81	7.64	60.72	26.24

Average K = 26.36×10^{-4}

TABLE 24

Molarity of Ketazine 0.01328. A = 18.14

T	X	A - X	% Hydrol.	K x 10 ⁴
57	2.24	15.90	12.35	(23.18)
107	4.56	13.58	25.14	27.10
163	6.50	11.64	35.83	27.24
203	7.80	10.34	43.00	27.72
241	8.98	9.16	49.51	28.37
280	9.85	8.29	54.30	27.98
318	10.43	7.71	57.50	26.92
358	11.06	7.08	60.97	26.30

Average K = 27.38×10^{-4}

TABLE 25

Molarity of Ketazine 0.01376. A = 18.80

T	X	A - X	% Hydrol.	K x 10 ⁴
58	2.39	16.41	12.71	(23.47)
102	4.43	14.37	24.11	26.37
144	5.97	12.83	31.76	26.55
188	7.29	11.51	38.78	26.24
234	8.98	9.82	47.77	27.70
276	9.94	8.86	52.87	27.27
311	10.76	8.04	57.23	27.32
390	12.16	6.64	64.68	26.70

Average K = 26.88×10^{-4}

SUMMARY

1. A brief survey of the literature on the stereo-isomerism in compounds containing the carbon-nitrogen double bond is presented.

2. The formation of ketazines from ketones and hydrazones in different media and under different conditions was investigated. No isomeric forms of p-methoxybenzophenone ketazine were detected.

3. Johnson's method for the study of the kinetics of hydrazone hydrolysis was adapted to the study of the hydrolysis of ketazines.

4. The rates of hydrolysis of benzophenone hydrazone and benzophenone ketazine were investigated under similar conditions and found to be approximately the same.

5. The rates of alpha and beta-p-methoxybenzophenone hydrazones and p-methoxybenzophenone ketazine were studied under similar conditions. In sufficiently high acid concentration these reactions are "pseudo" unimolecular, and show practically the same velocity of hydrolysis constant, K. Each of the substances hydrolyzed more rapidly and to the same extent in higher acid concentrations. We were unable to draw any further correlation between the acid strength of the medium and the rates obtained.

6. A theoretical discussion of the probable mechanisms of the three hydrolyses, including a common intermediate, is presented. Also a mechanism for the ketazine formation from the hydrazones is suggested.

